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Abstract: Background: Benign extrinsic obstruction of the hepatic duct, known as "Mirizzi syndrome" (MS), is an uncommon complication of longstanding cholelithiasis. Since laparoscopic cholecystectomy (LC) replaced the open approach, Mirizzi syndrome has regained the interest of biliary surgeons. Methods: The Swiss Association for Laparoscopic and Thoracoscopic Surgery (SALTS) prospectively collected the data on 13,023 patients undergoing LC between 1995 and 1999. This database was investigated with special regard to patients with Mirizzi syndrome. Results: There were 39 patients (14 men and 25 women; mean age, 61 years) with MS (incidence, 0.3%). Thirty-four patients had type 1 MS and five had type 2. A gallbladder carcinoma was found in four patients (incidence, 11%). In the type 1 group, 23 patients underwent cholecystectomy only, 10 patients had a bile duct exploration and T-tube insertion, and one patient had a Roux-en-Y reconstruction. In three patients with type 2, a hepaticojejunostomy was performed; two others underwent simple closure and drainage (via T-tube) of the biliary fistula. The conversion rate was 74% (24 of 34 patients) in the type 1 group and 100% (five of five patients) for type 2. The overall complication rate was 18%. There were no deaths. Conclusions: Although MS is rarely encountered during LC, it must be recognized intraoperatively. Conversion to an open approach is often needed, and prior to any surgical intervention, gallbladder cancer must be excluded

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SURGICAL ENDOSCOPY
and Other Interventional Techniques

Incidence and management of Mirizzi syndrome during laparoscopic cholecystectomy

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Abstract
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Methods: The Swiss Association for Laparoscopic and Thoracoscopic Surgery (SALTS) prospectively collected the data on 13,023 patients undergoing LC between 1995 and 1999. This database was investigated with special regard to patients with Mirizzi syndrome.
Results: There were 39 patients (14 men and 25 women; mean age, 61 years) with MS (incidence, 0.3%). Thirty-four patients had type 1 MS and five had type 2. A gallbladder carcinoma was found in four patients (incidence, 11%). In the type 1 group, 23 patients underwent cholecystectomy only, 10 patients had a bile duct exploration and T-tube insertion, and one patient had a Roux-en-Y reconstruction. In three patients with type 2, a hepaticojejunostomy was performed; two others underwent simple closure and drainage (via T-tube) of the biliary fistula. The conversion rate was 74% (24 of 34 patients) in the type 1 group and 100% (five of five patients) for type 2. The overall complication rate was 18%. There were no deaths.
Conclusions: Although MS is rarely encountered during LC, it must be recognized intraoperatively. Conversion to an open approach is often needed, and prior to any surgical intervention, gallbladder cancer must be excluded.

Key words: Laparoscopy — Cholecystectomy — Cholelithiasis — Mirizzi syndrome — Biliary fistula — Bile duct obstruction — Gallbladder cancer

Mirizzi syndrome (MS) is a benign mechanical obstruction of the hepatic duct caused by an impacted gallstone in the gallbladder neck and associated with longstanding inflammatory changes of the hepatoduodenal ligament. The first descriptions were published by Ruge [24] at the beginning of the 20th century. In 1948, Mirizzi reported a "functional hepatic syndrome" in patients with extrinsic compression of the common hepatic duct [18]. Although he erroneously assumed that mechanical compression and local inflammation induced a spasm of the hepatic duct, the clinical entity became known as "Mirizzi syndrome". Cholangitis and obstructive jaundice are the main clinical symptoms; however, a few patients show only mild or intermitant clinical signs due to partial obstruction.

The reported incidence of MS is low, ranging from 0.5% to 1.4%, but some ethnic populations, such as Native Americans (Navajo and Zuni heritage), have significantly increased incidences as high as 2.7% [1, 4, 7]. Since a variety of local anatomical changes may occur, several classification systems have been developed to assess the different subtypes of MS [2–6, 16, 19]. The classification proposed by McSherry in 1982, which differentiates between two types of MS, is currently in wide use [16]. Type 1 is characterized by extrinsic compression of the hepatic duct, whereas type 2 is associated with a cholecystocholedochal fistula. There is some evidence that MS may be associated with an increased coincidence of gallbladder cancer [20, 23]. It has been assumed that chronic inflammation and cholelithiasis lead to severe mucosal damage that is further linked to biliary cancer.

Laparoscopic cholecystectomy (LC) has almost completely replaced open cholecystectomy for the treatment of symptomatic gallstone disease. Previous contraindications—e.g., acute cholecystitist—are no longer considered valid reasons to exclude patients from undergoing the procedure via a laparoscopic approach. However, LC is particularly hazardous in patients with MS because the safe dissection of Calot's triangle is hampered by severe local inflammation and adhesions; thus, particular at-

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Table 1. Patient characteristics

	Overall group	Patients with MS
Patients (*n*)	13,023	39
Age (yr)		
Mean	51	61
Range	6–95	29–90
Indication (%)		
Symptomatic cholecystolithiasis	10,158 (78)	21 (54)
Acute cholecystitis	1,953 (15)	17 (43)
Others	912 (7)	1 (3)
MS known preoperatively		18 (46)

MS, Mirizzi syndrome

tention is needed to prevent bile duct injuries. Since laparoscopic bile duct exploration and repair have not been adopted by most laparoscopic surgeons as a standard treatment option, conversion to open bile duct exploration is often mandatory for the patient's safety.

The main purpose of this prospective study was to investigate the incidence and surgical management of MS in Switzerland in the era of laparoscopic surgery beyond the learning curve.

Patients and methods

Since 1995, the Swiss Association for Laparoscopic and Thoracoscopic Surgery (SALTS) has prospectively collected the data of patients undergoing various laparoscopic procedures from 110 institutions in Switzerland, with departments of general surgery (university, country, and district hospitals) as well as from surgeons in private practice. Approximately 7,000 laparoscopic operations are newly recorded every year. This huge database represents 60–75% of all laparoscopic procedures performed annually in Switzerland. For every patient, more than 130 single items, including personal records, American Society of Anesthesiologists (ASA) classification, indication for surgery, intraoperative findings, operative complications, conversion rate, postoperative morbidity, and mortality, were recorded on a specially designed computerized worksheet [26].

The data of 13,023 LC performed between January 1995 and December 1999 were analyzed, and all patients with MS were identified. Their medical records, operative reports, and an additional questionnaire, which was sent to the referring surgical institution or the general practitioner to obtain further details and follow-up data, were then carefully reviewed. If necessary, the institution or general practitioner was visited by one of the investigators to collect the missing data.

There are several classification systems of the subtypes of MS that are in clinical use. Following McSherry's classification, two types of MS were differentiated in the current study [16]. In type 1 MS, extrinsic bile duct obstruction is caused by an impacted gallstone in either the cystic duct or the ampulla of the gallbladder. In addition, there is a variable degree of inflammation around the hepatoduodenal ligament. Type 2 is characterized by the presence of a biliary fistula between the gallbladder and the common hepatic duct due to an ongoing destructive inflammatory reaction in the hepatoduodenal ligament.

Statistical analysis

Results are expressed as mean ± SD and range values, respectively.

Results

Characterization of patients and preoperative findings

The Swiss database included 13,023 LC for symptomatic gallstones (78%), acute cholecystitis (15%), and other reasons (7%). Most of the patients (90%) had a low-risk status (ASA 1 or 2 classification).

Table 2. Characteristics, preoperative findings, and indications of patients with Mirizzi syndrome

	Type 1 ($n = 34$)	Type 2 ($n = 5$)
Patients (*n*)	34	5
Male/female	10/24	4/1
Age (yr)		
Mean	63.5	62
Range	29–90	45–77
MS diagnosed preoperatively, *n* (%)	14 (41)	4 (80)
ERCP	8	3
MRCP	1	
US	2	
CT	1	1
IVC	2	
Clinical signs, *n* (%)		
RUQ pain	34 (100)	> 5 (100)
Fever	5 (15)	1 (20)
Jaundice	11 (32)	4 (80)
Laboratory findings *n* (range)		
Mean WBC count ($\times 10^9$/L)	8.8 (3.9–17.7)	11.5 (5.9–26.2)
Mean CRP (mg/L)	87 (2–386)	53 (9–100)
Mean ASAT (U/L)	71 (16–522)	149 (20–506)
Mean ALAT (U/L)	108 (12–770)	225 (13–777)
Mean AP (U/L)	154 (17–572)	482 (63–868)
Mean bilirubin (μmol/L)[a]	37 (4–192)	137 (12–425)
Indication		
Symptomatic cholecystolithiasis	18	3
Acute cholecystitis	15	2
Obstructive jaundice	1	
Emergency procedure	10	2
Elective procedure	24	3

RUQ, right upper quadrant; WBC, white blood cells (normal range, 3–5 × 10^9/L); CRP, C-reactive protein (normal, < 3 mg/L); AST, aspartate aminotransferase (normal, < 50 U/L); ALT, alanin aminotransferase (normal, < 50 U/L); AP, alkaline phosphatase (normal range, 30–115 U/L); ERCP, endoscopic retrograde cholangiopancreatography; MRCP, magnetic resonance cholangiopancreatography; US, ultrasonography; CT, computed tomography; IVC, intravenous cholangiography

[a] Bilirubin, normal < 25 μmol/L

As shown in Table 1, only 39 patients (14 male, 25 female) with a mean age of 61 years (range, 29–90) were found to have had MS (incidence, 0.3%). All patients presented preoperatively with right upper quadrant pain as the main clinical symptom; the two other symptoms that define cholangitis—jaundice and fever—occurred in only 21 patients (54%). One jaundiced patient underwent LC for suspected choledocholithiasis. Thirty-four patients (10 male, 24 female; mean age, 63.5 years) had type 1 MS (87%); the other five (four male, one female; mean age, 62 years) were classified as type 2 (13%). Although the MS had been diagnosed preoperatively in 18 patients (46%), the precise type could only be confirmed intraoperatively. The preoperative diagnosis of MS was made either by endoscopic retrograde cholangiopancreatography (ERCP) or radiological imaging (CT scan, ultrasonography, intravenous cholangiography) in 14 patients (41%) with type 1 and four patients (80%) with type 2.

Four of the five patients with type 2 were jaundiced, as were 11 of the 34 patients (32%) with type 1. The

Table 3. Operative findings, surgical procedures, intraoperative complications, and conversion rates

	Type 1 (n = 34)	Type 2 (n = 5)
Operative findings		
Compression of the common bile duct	34	
Cholecystocholedochal fistula		5
Gallbladder carcinoma (%)	4 (11.2)	
Surgical procedures		
Cholecystectomy	23	0
Cholecystectomy and T-tube drainage	10	3
Cholecystectomy and Roux-en-Y reconstruction	1	2
Intraoperative complications	2 (6)	1 (20)
Bile duct injury	1	
Duodenal laceration	1	
Bleeding		1
Conversion rate (%)	24 (71)	5 (100)

Table 4. Postoperative complications, reinterventions, and hospital stay

	Type 1 (n = 34)	Type 2 (n = 5)
Postoperative complications (%)	3 (8.2)	1 (20)
Bile leakage	1	
Intraabdominal abscess		1
Upper GI bleeding	1	
Pneumonia	1	
Reinterventions (%)	1 (2.9)	0
Relaparotomy	1	
Relaparoscopy		
Intervention (ERC, percutaneous drainage)		
Mortality	0	0
Hospital stay (d)		
Mean	12	18
Range	4–23	11–28

GI, gastrointestinal; ERC, endoscopic retrograde cholangiography

levels of laboratory parameters, particularly transaminases, alkaline phosphatase, and bilirubin, indicating cholestasis caused by extrahepatic bile duct obstruction, were significantly elevated preoperatively in type 2 patients. Since acute cholecystitis occurred more frequently in type 1 patients, their levels of C-reactive protein (CRP) were higher than those of type 2 patients.

The differences between patients with type 1 and those with type 2 are shown in Table 2.

Operative findings, surgical treatment, and intraoperative complications (Table 3)

MS was already suspected preoperatively in 18 patients, but surgical dissection of the hepatoduodenal ligament and the gallbladder was needed to confirm the precise diagnosis and subsequently enable the differentiation between simple external compression of the extrahepatic biliary system (type 1) or biliobiliary fistula (type 2). Four patients with type 1 MS were simultaneously found to have gallbladder cancer as an additional major finding (incidence, 11.2%). An early-stage tumor was found in two patients with dysplasia and pT1N0M0 cancer; the other two had advanced tumors (pT2N0M0 and pT3N1M0).

The overall conversion rate was 74%; conversion to an open approach was needed in 24 of the 34 patients with type 1 MS (71%) and all five of the patients with type 2. In most cases, local inflammatory changes made the dissection hazardous, and since laparoscopic bile duct exploration was not done routinely, the procedure was converted to ensure the patient's safety.

In 23 patients with type 1, surgical intervention was limited to cholecystectomy; another 10 patients underwent cholecystectomy and open bile duct exploration with T-tube insertion; a hepaticojejunostomy was performed in the final patient. All of the type 2 patients had open bile duct exploration. Three patients underwent a cholecystectomy and T-tube drainage; the other two needed a hepaticojejunostomy. Complete removal of the gallbladder was not possible in five patients (three type 1, two type 2), so only a subtotal cholecystectomy was performed. The overall intraoperative complication rate was 7.7%, with one bile duct injury, one duodenal laceration, and one incident of local bleeding.

Postoperative morbidity, mortality, and hospital stay (Table 4)

The overall complication rate was 10.3%. There were two surgical complications (one bile leak, one intraabdominal abscess) and two systemic complications (one upper gastrointestinal bleed, one case of pneumonia). One patient with gallbladder cancer underwent open reoperation, with common bile duct and liver wedge resection, and reconstruction with a Roux-en-Y hepaticojejunostomy. There were no deaths.

The mean hospital stay was 12 days for type 1 (range, 4–23) and 18 days (range, 11–28) for type 2.

Discussion

The purpose of this study was to investigate the incidence, preoperative diagnosis, and surgical management of MS in the era of LC beyond the learning curve. In addition, the coincidence of gallbladder cancer and MS was assessed. The data from this series show that MS is an uncommon clinical entity with an incidence of $<0.5\%$ and that its preoperative assessment remains difficult. Conversion to an open approach is often needed so that a precise identification of the anatomical structures can be made and a safe repair can be completed. In contrast to other reports in the literature citing alarmingly high rates (Radaelli et al. [23]), the incidence of simultaneous gallbladder cancer in this series was 11%.

The true incidence of MS remains unknown, because most of the cases that are diagnosed occur in symptomatic patients undergoing biliary surgery, while others may go undetected. Moreover, only case reports and small series can be found in the literature, and there is no difference between the open and laparoscopic era in

the rate of its detection [1, 2, 4, 5, 7, 8, 12, 14, 22, 25, 27–30]. In these reports, the incidence of MS ranged from 0.4% to 2.53% [1, 2, 4, 5, 7, 12, 14, 25, 27–29].

Several classification systems have been developed to distinguish between different types of MS. Involvement of the hepatic duct via the destruction of its wall or simple external compression is the most important criterion. One of the most widely accepted and simple classifications was proposed by McSherry, who defined type 1 as extrinsic compression of the hepatic duct and type 2 as the presence of a cholecystocholedochal fistula [16]. Type 2 was further divided into several subtypes by Csendes et al. and Nagakawa et al. based on the extent of the destruction of the hepatic duct [6, 19]. The goal of all of these classification systems is to enable the surgeon to tailor the surgical approach to the individual case. In type 1, MS, only cholecystectomy (total or subtotal) is needed; whereas patients with type 2 always require bile duct exploration with intraoperative cholangiography, as well as extrahepatic bile duct reconstruction via closure of the fistula and T-tube insertion, or bilioenteric anastomosis in cases with large defects. Since the preoperative diagnosis is difficult to establish, and surgical experience is a critical factor in the success of bile duct repair, the more sophisticated classification systems proposed by Csendes et al. and Nagakawa et al. probably do not provide an significant help to the general surgeon. If a cholecystocholedochal fistula is already suspected preoperatively the patient should be referred to a hepatobiliary surgical center. Only meticulous dissection of the hepatoduodenal ligament will reveal the extent of bile duct defect and thus determine the appropriate reconstruction technique.

Right upper quadrant pain was the most common preoperative clinical symptom, occurring in all patients. Whereas 80% of patients with type 2 MS were clinically jaundiced, only one-third of patients with type 1 presented with extrahepatic bile duct obstruction. A wide range of serum bilirubin levels was seen, and mean values were increased significantly only in type 2 patients. Fever occurred only rarely; therefore, neither type 1 nor type 2 was frequently associated with Charcot's trias, indicating cholangitis. In most series in the literature, pain was the predominant clinical symptom in all cases; however, in contrast to this study, jaundice was generally as frequent as pain, occurring in 60–100% of patients [5, 7, 12, 14, 25, 29].

In addition to a routine preoperative workup including laboratory findings and ultrasonography, ERCP was performed in 28% of patients to further investigate for obstructive jaundice and suspected MS. Intravenous cholangiography, CT scan, and magnetic resonance cholangiopancreatography (MRCP) were limited to a few cases. Although ultrasound is the most widely used radiological imaging technique, its predictive value for the identification of MS remains low [7, 10, 12]. ERCP is actually still the most reliable modality for the investigation of the extrahepatic biliary system [1, 12, 14, 29, 31]. In our series, only 40% of the type 1 MS were diagnosed preoperatively; the other 60% required an operative exploration for final confirmation. In contrast, four of the five type 2 cases were already known preoperatively due to the presence of biliary obstruction. If the patient does not present with complete external bile duct obstruction, as is typically seen in gallbladder cancer, the preoperative diagnosis of type 1 MS is difficult because ERCP is restricted to patients with jaundice and/or elevated liver function tests. To compound the difficulty, intravenous cholangiography has been largely abandoned in the laparoscopic era.

Surgical treatment options include a broad variety of procedures and approaches. Predominantly in type 1, cholecystectomy and stone removal from the cystic duct are usually performed. Due to the unclear anatomical situation, dissection from the fundus toward Hartmann's pouch and subtotal removal of the gallbladder are advocated as a safe and effective treatment option that obviates the risk of major bile duct injury [1, 12]. In type 2, bilioenteric anastomosis is needed in cases where a large circumferential defect and/or cholecystocholedochal fistula is present. Limited common bile duct defects can be closed directly with a T-tube drain. Surgical techniques that use gallbladder flaps to cover large bile duct defects have been shown to be associated with an increased complication rate and have therefore been abandoned [1, 11, 31]. Finally, a laparoscopic procedure is usually attempted, but conversion to an open approach is favored by most experienced surgeons [8, 11, 12, 30].

Gallbladder cancer is a rare disease in Western countries that is strongly associated with longstanding cholelithiasis and chronic cholecystitis [9, 15]. Although MS and gallbladder cancer have similar risk factors as mentioned previously (long-standing cholelithiasis, chronic cholecystitis), there are only a few reports describing the coincidence of gallbladder cancer in patients with MS [17, 21, 23]. Whereas Redaelli et al. reported an alarming coincidence of 28%, the rate of cancer in our series was 11% [23]. A strong association between MS and gallbladder cancer can therefore be assumed. For the reason, frozen sections should be obtained from all patients undergoing surgery for MS. Since the prognosis of patients with gallbladder cancer is dismal, an accurate diagnosis followed by radical open surgical treatment provides their best hope.

The postoperative morbidity and mortality rates were $< 10\%$ and zero, respectively, and most complications were minor (e.g., bile leakage). The fact that the surgical treatment of MS can be performed safely is also confirmed by most of the reports in the literature, with few complications and nearly no deaths [2, 5, 7, 11, 12, 28, 29].

In conclusion, MS is a rare complication of longstanding cholelithiasis with a low incidence; however, laparoscopic surgeons must be wary. The preoperative diagnosis is not of utmost importance, but its intraoperative recognition and a low threshold for conversion to open bile duct exploration are crucial to the long-term outcome. Because there is strong evidence that the incidence of simultaneous gallbladder cancer is significantly increased, frozen sections must be obtained to exclude the presence of local malignancy prior to closure or bile duct reconstruction.

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